Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendments, claims 45, 46, 48-57, 59-64 and 67-73 are pending in the application, with claims 45, 54 and 64 being the independent claims. Claims 45, 48, 54, 55, 59, 64 and 67 are sought to be amended by the present amendment. Claims 1-6, 12 and 74-77 are sought to be cancelled by the present amendment without prejudice to or disclaimer of the subject matter therein. Claims 7-11, 13-44, 47, 58 and 65-66 were previously cancelled without prejudice to or disclaimer of the subject matter therein.

Claims 45, 48, 54, 55, 59, 64 and 67 have been amended to further clarify Applicants' invention. In the Markush group defining the CYK-4 protein, claim 45 has been amended to substitute "protein" with "polypeptide" and to insert thereafter the phrase " which stimulates GTP hydrolysis by the Rho family GTPase and which has" immediately prior to "an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1" and prior to "an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3." Claim 48 has been amended accordingly to reflect this change.

Claims 54 and 64 have also been amended in a similar manner, except that the phrases " which binds the MKLP1 protein subfamily member" and "which binds to the first CYK-4 protein or the second CYK-4 protein" have been inserted, respectively. Claims 59 and 67 have been amended accordingly.

Support for these changes can be found in the specification, e.g., at page 20, lines 15-26; at page 28, lines 7-10; at page 31, line 13, to page 32, line 6, and in Example 8, at pages 67-69; and at page 33, lines 18-25, and in Example 11, at pages 75-77.

Claims 45, 54 and 64 have also been amended to delete text reciting that the CYK-4 protein or fragment comprises a GTPase activating protein domain, a domain that binds MKLP1 subfamily proteins, or a domain that mediates CYK-4 protein self-association, respectively. Claim 55 has also been amended to delete the phrase "comprises a domain that."

These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Rejection under 35 U.S.C. § 112, First Paragraph, Scope of Enablement

The Examiner rejects claims 45, 46, 48-57, 59-64 and 67-73 under 35 U.S.C. § 112, first paragraph, for an alleged lack of enablement. (Office Action, at page 2, lines 12-13.)

Specifically, the Examiner states:

> The specification does not provide sufficient guidance and/or working examples to make those variants that have the same functional activity as human CYK-4 of SEQ ID NO: 2 and murine CYK-4 protein of SEQ ID NO: 4 and to use those variants that do not have the same functional activity as human CYK-4 of SEQ ID NO: 2 and murine CYK-4 protein of SEQ ID NO: 4 . . . . Moreover, the state of the art is such that determining the specificity of

> hybridization is empirical by nature and the effect of mismatches is unpredictable, as taught by Wallace et al. . . . and Sambrook et al. . . . . It is well known in the art that hybridisation yields structurally related, but functionally different nucleic acids. Thus, it would take undue experimentation for one skilled in the art to make and use the claimed methods.

(Office Action, at page 3, lines 7-20.)

In order to satisfy 35 U.S.C. § 112, first paragraph, Applicants must provide sufficient guidance so that one of ordinary skill in the art can make and use the claimed invention. The amount of enabling disclosure must be such that a person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

In determining whether a patent application satisfies the enablement requirement under 35 U.S.C. § 112, first paragraph, the Federal Circuit held that "[e]nablement is not precluded by the necessity for some experimentation such as routine screening." *In re Wands*, 858 F.2d 731, 736-737 (Fed. Cir. 1988). However, the experimentation cannot be undue. *Id.* The Federal Circuit also held that "[t]he determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art." *Id.* at 737 (quoting *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (Bd. Pat. App. 1982)). The court states that "[t]he test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Id.*

Applicants assert that they have provided sufficient guidance in the specification to have enabled one of ordinary skill in the art, at the time of filing of the application, to make the CYK-4 protein variants and use them in the claimed methods without undue experimentation, and that the present application enables the full scope of the claims as currently presented.

The claimed methods recite that the CYK-4 variants are produced by hybridization using polynucleotides having the sequences shown in SEQ ID NO:1 and SEQ ID NO:3, both of which are defined sequences provided in the specification.

Nucleic acid hybridization techniques to produce the CYK-4 protein variants of the claimed methods were well known to those of ordinary skill in the art at the time of filing of the application. See, for example, Sambrook *et al.*, Molecular Cloning, a Laboratory Manual, 2nd Ed., Cold Spring Harbor Laboratory Press (1989), at Chapter 11, especially page 11.45. Applicants note that the date of publication of this reference (cited also by the Examiner) is ten or eleven years prior to the earliest priority date of the current application, which is June 19, 2000. Sambrook, and other manuals available at the time of filing of the application, provide detailed guidance on how to perform the recited hybridization techniques.

Moreover, the claims at issue recite the specific stringent hybridization conditions required for isolating the recited CYK-4 protein variants, eliminating the need for one of skill in the art to empirically determine the hybridization conditions required to produce the CYK-4 variants of the claimed methods. The specification also sets out the same specific stringent hybridization conditions at page 21, lines 14-21. The Examiner's statement that "determining the specificity of hybridization is empirical by nature . . . ."

does not apply in light of the hybridization conditions recited in the claims and provided in the specification.

Applicants note that use of hybridization language is a standard and accepted way of claiming a reasonable number of polynucleotide or polypeptide variants. See, e.g., the U.S. Patent and Trademark Office's written description guidelines training manual, entitled "Synopsis of Application of Written Description Guidelines," Example 9, pp. 35-37 (www.uspto.gov/web/menu/written.pdf), which is discussed in more detail below in Applicants' response to the written description rejection.

Thus, the specification, together with the general knowledge available in the art, would have provided sufficient guidance to one of ordinary skill in the art to make the CYK-4 protein variants of the claims without undue experimentation. The nucleic acid hybridization techniques needed to produce the CYK-4 variants were well known in the art, and the level of skill of one of ordinary skill in the art was high with respect to hybridization techniques. In addition, a person skilled in the art would have been able to make the CYK-4 protein variants of the claims using routine hybridization techniques, without any additional experimentation to establish the specific hybridization conditions sufficient to produce the CYK-4 protein variants.

The claims as presented also require that the CYK-4 protein variants possess the biological activity relevant to the claimed screening method. Specifically, the Markush group defining the CYK-4 protein in claims 45, 54 and 64 recite that the CYK-4 variant stimulates GTP hydrolysis by the Rho family GTPase used in the recited method (*i.e.*, retains the CYK-4 GTPase activating protein ("GAP") activity) (claim 45), that the CYK-4 variant binds the MKLP1 protein subfamily member used in the recited method

(claim 54), and that the CYK-4 variant binds to the first CYK-4 protein or the second CYK-4 protein used in the recited method (claim 64).

Again, no undue experimentation would have been required to screen the CYK-4 variants for the required activity. Assays that can be used to determine whether the CYK-4 variants possess each of these activities were known to those of skill in the art at the time of filing of the application and are routine. The specification also provides several examples of these assays. For example, the "GTP hydrolysis assay" is a standard assay that can be used to screen for functional CYK-4 variants that retain GAP activity. See the specification, e.g., at page 27, lines 20-25. The specification also provides examples of the assay, e.g., at page 45, lines 15-28; and at page 27, line 25, to page 30, line 2 (conducting the assay in the absence of test compound). Examples of assays that can be used to assess the ability of the CYK-4 variants to bind a MKLP1 protein subfamily member or to self-associate can be found in the specification as well, e.g., at page 61, lines 3-31; in Examples 7-9 at pages 65-70; and at page 30, line 8, to page 34, line 20 (conducting the assay in the absence of test compound).

Lastly, the specification also provides detailed examples of how to use the CYK-4 protein variants in the claimed methods. See, e.g., the specification, at page 27, line 3, to page 34, line 20.

Thus, Applicants believe that, contrary to the Examiner's assertion, it would not have taken undue experimentation for one skilled in the art to make the CYK-4 protein variants and use them in the claimed methods.

With respect to the Examiner's statement that the specification does not provide sufficient "working examples" to make those variants that have the same functional

activity as human CYK-4 and murine CYK-4 (Office Action, at page 3, lines 8-9), Applicants note that it is long settled case law that Applicants are not required to provide objective evidence in the form of working examples to enable the claimed invention. *In re Marzocchi*, 439 F.2d 220, 223 (C.C.P.A. 1971).

The Examiner also states that "the specification . . . does not disclose the GTPase activating protein domain and the domain that binds MKLP1 subfamily proteins." (Office Action, at page 4, lines 8-9.) The Examiner further states that "neither the specification discloses nor the claims recite a defined functional domain for the CYK-4 protein, fragment, or variant," and that "[r]eciting a function for a fragmet [sic] or a variant without defining the structural domain does not provide sufficient guidance for one [of] skilled in the art to make the functional fragment or variant." (Office Action, at page 4, lines 16-19.)

To expedite prosecution and without acquiescing in the propriety of the rejection, Applicants have amended claims 45, 54 and 64 to delete text reciting that the CYK-4 protein or fragment comprises a GTPase activating protein domain, a domain that binds MKLP1 subfamily proteins, or a domain that mediates CYK-4 protein self-association, respectively, thereby rending moot this ground of rejection.

Applicants believe that they have provided sufficient guidance for one of ordinary skill in the art to make and use the CYK-4 proteins and fragments recited in the claimed methods at issue without undue experimentation and that the present application enables the full scope of the claims as currently presented.

Thus, Applicants believe that the rejection of claims 45, 46, 48-57, 59-64 and 67-73 under 35 U.S.C. § 112, first paragraph (scope of enablement), has been overcome and respectfully request that the Examiner reconsider and withdraw this rejection.

II. Rejections under 35 U.S.C. § 112, First Paragraph, Written Description

The Examiner rejects claims 45, 46, 48-57, 59-64 and 67-73 under 35 U.S.C. § 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. (Office Action, at page 5, lines 7-10.)

Specifically, the Examiner states that "neither the specification discloses nor the claims recite a functional domain for the CYK-4 protein, fragment, or variant." (Office Action, at page 5, lines 17-18.)

As discussed earlier, to expedite prosecution and without acquiescing in the propriety of the rejection, Applicants have amended claims 45, 54 and 64 to delete text that recites that the CYK-4 protein or fragment comprises a GTPase activating protein domain, a domain that binds MKLP1 subfamily proteins, or a domain that mediates CYK-4 protein self-association, respectively, rendering moot this basis for rejection.

The Examiner also states with respect to the recited CYK-4 proteins, fragments and variants that "[i]t is noted that only description of what a compound does without disclosure of the chemical structure of the compound, as is the case here, is not sufficient to satisfy the written description requirement under 35 U.S.C. § 112, first paragraph." (Office Action, at page 5, line 18, to page 6, line 3.)

To expedite prosecution and without acquiescing in the propriety of the rejection, Applicants have amended the Markush group defining the CYK-4 protein in claims 45, 54 and 64 to recite that the CYK-4 variant produced by hybridization stimulates GTP hydrolysis by the Rho family GTPase used in the recited method (*i.e.*, retains the CYK-4 GTPase activating protein ("GAP") activity) (claim 45), binds the MKLP1 protein subfamily member used in the recited method (claim 54), and binds to the first CYK-4 protein or the second CYK-4 protein used in the recited method (claim 64).

Applicants believe that one of skill in the relevant art would recognize that the Applicants were in possession of the full scope of the claimed methods as presented.

To fulfill the written description requirement of 35 U.S.C. § 112, first paragraph, a patent specification must describe an invention in sufficient detail that one skilled in the art can clearly conclude that the inventors invented the claimed subject matter. *See Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404 (Fed. Cir. 1997). Stated differently, the written description requirement is satisfied when the specification "set[s] forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed." *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 928, 69 U.S.P.Q.2d 1886, 1896 (Fed. Cir. 2004). Moreover, an important consideration in assessing written description of a claimed invention is the knowledge of one skilled in the art. *See Bilstad v. Wakalopulos*, 386 F.3d 1116, 1126, 72 U.S.P.Q.2d 1785, 1792 (Fed. Cir. 2004).

The claims as presented recite methods of determining whether a compound has the potential to inhibit cytokinesis by determining the compound's ability to inhibit a

function of a CYK-4 protein or fragment thereof. The claims recite that the CYK-4 protein is a protein having the sequence of SEQ ID NO:2 or SEQ ID NO:4 or is a polypeptide that is produced by hybridization using polynucleotides having the sequences shown in SEQ ID NO:1 or SEQ ID NO:3 and possesses the particular activity measured in the method. CYK-4 protein or fragment must also possess the particular activity measured in the assay in the absence of the compound.

Applicants respectfully submit that, in the current case, disclosure of the exact chemical structures of all the recited CYK-4 proteins and variants is not required in order to satisfy the written description requirement because the specification, coupled with the knowledge available in the art, sufficiently describes the genus of CYK-4 proteins and protein variants of the claimed methods so that a person of ordinary skill in the art could visualize and/or recognize members of the CYK-4 protein genus and recognize that Applicants were in possession of the full scope of the claimed methods.

With respect to the CYK-4 protein variants of the genus, the recited stringent hybridization conditions, in combination with the recited hybridization templates of defined sequence (SEQ ID NOs:1 and 3), would produce structurally related CYK-4 polynucleotides. As discussed above, the nucleic acid hybridization techniques needed to produce the CYK-4 variants were well known in the art at the time of filing of the application, and the level of skill of one of ordinary skill in the art was high with respect to hybridization techniques. In addition, the functional activity required for the CYK-4 proteins and variants would ensure that the CYK-4 polypeptides of the genus possess the relevant activity. Thus, a person of ordinary skill in the art would be able to visualize and/or recognize the CYK-4 protein variants of the genus.

Applicants note that claims using hybridization language similar to that in the claims at issue have been considered by the U.S. Patent and Trademark Office to satisfy the written description requirement. See, e.g., the written description guidelines training manual used by the U.S. Patent and Trademark Office ("PTO"), "Synopsis of Application of Written Description Guidelines," Example 9, pp. 35-37 (www.uspto.gov/web/menu/written.pdf). Example 9 addresses whether the written description requirement is satisfied for a claim directed to an isolated nucleic acid that specifically hybridizes under stringent conditions a defined nucleic acid sequence and encodes a protein with a specific function, a claim similar to the claims at issue in the current application. The example concludes:

> Now turning to the genus analysis, a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.

Id., at page 36. Thus, Example 9 illustrates that claims reciting hybridization language, when coupled with function, are considered by the PTO as satisfying the written description requirement.

The specification also discloses the complete sequences of the remaining two members of the CYK-4 protein genus (the murine and human CYK-4 polypeptide sequences SEQ ID NO:1 and SEQ ID NO:4) and would allow one of skill in the art to recognize these members of the genus.

Thus, the specification, coupled with the knowledge available in the art, sufficiently describes the genus of CYK-4 proteins and protein variants recited by the claimed methods so that a person of ordinary skill in the art could visualize and/or recognize members of the recited CYK-4 protein genus.

In addition, the specification provides details on how to carry out each method using the CYK-4 proteins and variants and includes a detailed discussion of each of the claimed methods. See, e.g., the specification, at page 28, lines 7-10; at page 31, line 13, to page 32, line 6, and in Example 8, at pages 67-69; and at page 33, lines 18-25, and in Example 11, at pages 75-77.

Thus, Applicants submit that the specification, coupled with the knowledge available in the art, sufficiently describes the claimed methods so that a person of ordinary skill in the art would recognize that Applicants were in possession of the full scope of the claimed methods at the time of filing of the application.

Applicants believe that the rejection of claims 45, 46, 48-57, 59-64 and 67-73 under 35 U.S.C. § 112, first paragraph (written description), has been overcome and respectfully request that the Examiner reconsider and withdraw this rejection.

III. Claim Objections - Minor Informality

The Examiner maintains the previous objection to claims 45, 46, 51-57, 60-64 and 67-73 as reciting non-elected subject matter (murine CYK-4 of SEQ ID NO:4). (Office Action, at page 6, lines 5-7.)

Applicants note that in the Office Action dated February 23, 2005, the Examiner agreed to examine all generic linking claims, including the search and examination of

claims reciting murine SEQ ID NO:4, if a generic claim is allowed. Accordingly, Applicants respectfully request that the Examiner withdraw the objection and consider all generic linking claims that encompass murine CYK-4 under 37 C.F.R. § 1.141(a).

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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